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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,099	04/07/2004	Simon McEwen	61190(50221)	8281

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EDWARDS ANGELL PALMER & DODGE LLP  
P.O. BOX 55874  
BOSTON, MA 02205

EXAMINER
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HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
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1651

MAIL DATE	DELIVERY MODE
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10/15/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/820,099

Applicant(s)

MCEWEN, SIMON

Examiner

Susan Hanley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 25-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-24 and 29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>20071004</u>                             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                           |

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## DETAILED ACTION

### *Election/Restrictions*

The requirement mailed 08/02/07 has been vacated. Applicant's election with traverse of Group I, claims 1-24 and 29; and mucopolysaccharidases as the enzyme specie in the reply filed on 4/5/07 is acknowledged. Claim 29 was inadvertently placed in Group II. The traversal is on the ground(s) that the groups represent a single inventive concept and that the search for both groups does not represent a burden to the examiner. This is not found persuasive because it was shown in the restriction requirement that the inventions of groups I and II are distinct because the composition has uses other than that which is claimed, e.g., treating an auto-immune disease. Hence, the groups are not represented by a single searchable concept.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/5/07.

Claims 1-24 and 29 are presented for examination.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-24 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

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the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a therapeutic composition for the treatment or prophylaxis of an autoimmune condition wherein the composition comprises an effective amount of an enzyme and an immunogen. Dependent claims define the enzyme as a beta-glucuronidase, the immunogen can be collagen, the composition can further comprise a stabilizer and/or activator as well as compounds that contain hydroxyl moieties.

The specification speculates that claimed composition down-regulates T-cell mediated reactions. The specification asserts that the claimed composition can treat or prevent auto-immune diseases including rheumatoid arthritis (RA). An example of the efficacy of the claimed composition in a mouse model of RA is disclosed. Three groups of mice were injected with collagen. Groups A and C were treated with different strengths (group C receiving the higher dose) of the claimed composition while group B served as the control. The severity of the response to the collagen injection was by observation. The specification discloses that early on, the mice in group A had a somewhat lower incidence of the disease, and after day 29 there was no significant difference between the control and the lower dose treatment group. The specification discloses that the higher dose group (group C) displayed a lower severity of RA during the time course compared to the control and the levels of disease reaction are "within the range seen when established anti-arthritic drugs are given during the course of similar experiments" (p. 13). An Anova analysis of groups B vs. C was on the order of  $p=0.0196$ .

The disclosure has been carefully considered but it is not deemed as enabling the claims. The claimed composition and its intended use for treating auto-immune diseases is an extension of enzyme-potentiated desensitization (EPD) which was developed by McEwen in the 1970's for allergy

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treatment. EPD and other forms of immunotherapy were recently reviewed by Terr (2004). Terr notes that proponents of EPD claim that it has successfully treated allergic rhinitis as well as ulcerative colitis, IBS, chronic fatigue syndrome, hyperactivity, rheumatoid arthritis, etc. (p. 707). However, Terr asserts that "To date, there have been no published research finding in patients treated by this method to substantiate this theory. The effectiveness of enzyme-potentiated desensitization and the presumed pharmacological property of beta-glucuronidase on the immune system are based on anecdotal evidence only. Several published double-blind reports claim symptomatic improvements in adults or children with allergic rhinitis or asthma along with conflicting results of immunological changes. These studies have been done on 10 to 20 subjects only in the active and placebo groups, have been of short duration and generally lacked objective measurements of disease activity" (p. 707). Terr goes on to enumerate the numerous rules to avoid treatment failure. In a similar review in 1999, Terr noted that there were no published studies to substantiate the hypothesis of the action of EPD on the immune system, wherein proponents of EPD assert that the therapy activated a new population of CD8 lymphocytes that suppress or down-regulate the response to injected patients, thereby suppressing the immune response (p. 484).

Claims drawn to pharmaceutically acceptable compositions and to methods of administering said compositions to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments. EPD has been reviewed in the literature and clear-cut evidence regarding its efficacy is not convincing. The instant application is an extension of EPD from its origin for the treatment of allergic rhinitis to the therapy of auto-immune diseases. The data provided by the examples does not substantiate the claims. There is no substantial difference between the control group and those mice receiving the lower dose (group A). The data

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regarding groups B and C is not clear cut. The calculated correlation factor is low and the data in Figures 3 and 5 shows a great deal of overlap of data points. The specification relies on a nebulous conclusion (e.g., comparing the disclosed data with undisclosed data for unnamed RA treatments). Thus, the data presented by the specification does not appear to be a reliable indicator that the skilled artisan could use to predict successful therapeutic outcome for a patient group that is known to be extremely difficult to treat. Furthermore, the review of human treatment records by the prior art casts doubt on EPD, in general.

There is no reliable method that predicts if EPD is effective in treating for preventing autoimmune diseases, including RA. The disclosure cannot be extrapolated by the skilled artisan to predict if EPD will be effective to treat or prevent autoimmune diseases. It would require one of skill in the art undue experimentation to determine if EPD would be effective for the claimed treatment according to the directions of the instant disclosure. Thus, the claims are not enabled by the disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley  
Patent Examiner  
Art Unit 1651

SANDRA E. SAUCIER  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Sandra E. Saucier', written over the printed name and title.